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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/549,937	04/14/2000	Michael B Chancellor	2710-4007US2	9119

7590 03/11/2003

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EXAMINER
WHITEMAN, BRIAN A

ART UNIT	PAPER NUMBER
1635	14

DATE MAILED: 03/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/549,937	CHANCELLOR ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-26,28-54,56-93 and 96-106* is/are pending in the application.

4a) Of the above claim(s) *4-16,28-44,56-83,85-91 and 97-99* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,17-26,45-54,84,92,93,96 and 100-106* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *21 November 2002* is: a)☒ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *13* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Final Rejection

Claims 1, 3-26, 28-54, 56-93, and 96-106 are pending.

Applicants' traversal, the amendment to claims 1, 84, and 96, the amendment to the specification, the cancellation of claims 2, 27, 55, 94, and 95, and the addition of claims 100-106 in paper no. 12 is acknowledged and considered.

This application contains claims 4-16, 28-44, 56-83, 85-91, 97-99 drawn to an invention non-elected with traverse in Paper No. 7. A complete reply to the final rejection must include cancellation of non-elected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Drawings

Color photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) is granted permitting their use as acceptable drawings. In the event that applicant wishes to use the drawings currently on file as acceptable drawings, a petition must be filed for acceptance of the color photographs or color drawings as acceptable drawings. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and an amendment to the first paragraph of the brief description of the drawings section of the specification which states:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the U.S. Patent and Trademark Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1, 3, 17-26, 45-54, 84, 92-93, and 96 remain and claims 100-106 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 3, 17-26, 45-54, 84, 92, 93, 100-106, as best understood, are readable on a genus of an isolated mammalian muscle-derived progenitor cells (MDC) having a long term survivability when introduced into mammals recipient host, wherein the long-term survivability is determined by viability or proliferation of the cells as muscle tissue cells at or near a site of introduction for greater than or equal to about two weeks following subcutaneous injection into (i) a severe combined immune deficient (SCID) mouse model system or (ii) the recipient host, wherein the genus of progenitor cells is not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 and 96, as best understood, are readable on a genus of an isolated mammalian muscle-derived progenitor cells (MDC) having a long term survivability when introduced into mammals recipient host, wherein the long-term survivability is determined by viability or proliferation of the cells as muscle tissue cells at or near a site of introduction for greater than or equal to about two weeks following subcutaneous injection into (i) a severe combined immune deficient (SCID) mouse model system or (ii) the recipient host, and wherein the cells express cell markers selected from the group consisting of CD34, Bcl-2, Sca-1 and Flk-1 and do not express CD45 and c-kit cell markers, wherein the genus of cells is not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification contemplates a genus of an isolated mammalian MDCs having a long term survivability when introduced into mammals recipient host, wherein the long-term survivability is determined by viability or proliferation of the cells as muscle tissue cells at or near a site of introduction for greater than or equal to about two weeks following subcutaneous injection into (i) a severe combined immune deficient (SCID) mouse model system or (ii) the recipient host. The as-filed specification provides sufficient description of a species of isolated cells (pp6) from a mouse having long-term survivability. The examples in the specification

isolate cells (pp6) from mdx mice, female SD rats and SCID mice. The pp6 cells were examined by immunohistochemical analysis by the expression of cells markers (pages 29-30, Table 1). The pp6 cells displayed several markers (see Table 1), including Flk-1 a mouse homologue of human KDR gene, which was recently identified as a marker of hematopoietic cells with stem-like characteristics. Furthermore, the pp6 display a CD34 marker and the art of record teaches that although the reversible expression of CD34 remains to be determined in muscle derived stem cells, the use of CD34 as a marker of muscle-derived stem cells should at least by used with caution. The art of record displays the variability of murine muscle-derived progenitor cells, see Qu et al. Journal of Cell Biology, Vol. 142, pp. 1257-1267, 1998 (IDS) and Lee et al., The Journal of Cellular Biology, Vol. 150, 2000, pp. 1085-1099. The art of record further teaches that a recent report has suggested that only a discrete minority of myoblast can survive after implantation and thus may represent a population of myogenic stem cells (See Lee).

Furthermore, the disclosure does not provide an adequate written description of a representative number of species of isolated mammalian muscle-derived progenitor cells, which functions as intended in the claimed invention. It is not apparent from the specification that the description of phenotypic markers is essential for the biological function of the muscle-derived progenitor cells having long term survivability. The structure that is required for an adequate description of a representative number of species as embraced by the claimed genus of isolated mammalian muscle-derived progenitor cells is not described sufficiently in the specification. As stated above, a mere statement asserting that any cell having the phenotypic markers without providing the essential elements does not lend evidentiary support for a skilled artisan to have recognized that the applicant was in possession of the genus of cells having a phenotype as

claimed, particularly since the skill and knowledge in the art is not adequate to determine the structure of the representative number of species of mammalian muscle-derived progenitor cells that is essential for the biological function as intended by the claimed invention on the basis of the disclosure of only one species consisting of an isolated murine muscle-derived progenitor cells.

It is apparent that on the basis of applicant's disclosure, an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the invention and reference to potential methods and/or molecular structures of cells that are essential for a genus of an isolated mammalian muscle-derived progenitor cells as claimed; what is required is the knowledge in the prior art and/or a description as to the availability of a representative number of species of biochemical or molecular structures of a genus of isolated MDCs that must exhibit the disclosed biological functions as contemplated by the claims.

It is not sufficient to support the present claimed invention directed to a genus of isolated mammalian muscle-derived progenitor cells expressing desmin as a cell surface protein and having long-term survivability when introduced into an autologous or allogeneic mammalian recipient. The claimed invention as a whole is not adequately described if the claims require essential or critical elements, which are not adequately described in the specification and which is not conventional in the art as of applicant's effective filing date. Claiming a genus of isolated mammalian muscle-derived progenitor cells that must possess the biological properties as contemplated by applicant's disclosure without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of*

the Univ. Calif. v. Eli Lilly & Co., 43 USPQ2d 1398 (CA FC, 1997)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a genus of isolated mammalian muscle-derived progenitor cells that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Applicant's arguments filed 11/21/02 have been fully considered but they are not persuasive. The specification only provides sufficient description of pp6 cells from murine or rats. The specification contemplates a means to assess whether isolated MDC are viable and proliferate and survive as claimed by injecting into SCID mice and assessing whether the cells are viable for muscle tissue cells at a time of at least two weeks after injection. However, in view of the art of record, the contemplation displays that applicants did not have possession of a representative number of isolated mammalian muscle-derived progenitor cells to represent the claimed genus. The traversal (see page 8, bottom) displays that the specification was not in possession of a representative number of species of the claimed isolated mammalian muscle-derived progenitor cells to support the genus of claimed MDCs to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Declaration of Michael Chancellor, M.D. under 37 CFR 1.132 filed 11/21/02 is insufficient to overcome the rejection of claims 1, 3, 17-26, 45-54, 84, 92-93, 96, and 100-106 based upon 112 first paragraph written description as set forth in the last Office action because: the specification only teaches how to isolate or obtain the claimed MDC from explants of mdx and SCID mice and SD female rats. The declaration (see pages 2-3 and 8) displays that the specification was not in possession of a representative number of species of the claimed isolated mammalian muscle-derived progenitor cells to support the genus of claimed MDCs to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 3, 17-26, 45-54, 84, 92-93, and 96 remain and claims 100-106 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated murine muscle-derived progenitor cells, wherein the cells are pp6 and express cell markers selected from the group consisting of desmin, CD34, Sca-1, Flk-1, and Bcl-2 and do not express CD45 and c-Kit and using the cells in a method of augmenting or bulking muscle in a rat or a mouse; and isolated clonal murine muscle-derived progenitor cells (mc13), wherein the clonally isolated cells express desmin, Flk-1, Sca-1 and does not express CD34, CD45, and c-Kit and does not reasonably provide enablement for a genus of an isolated muscle-derived progenitor cells having long-term survivability and any therapeutic method contemplated by the claimed invention. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to make and/or the invention commensurate in scope with these claims.

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Specifically, since the claimed invention is not supported by a sufficient written description (for possession of a genus of an isolated muscle-derived progenitor cells having long-term survivability) particularly in view of the reasons set forth above, one skilled in the art would not have known how to use and make the claimed invention so that it would operate as intended, e.g. for use in a method of augmenting or bulking muscle tissue in a mammalian host.

The art of record for cell transplantation (e.g. myoblast) has been hindered by various limitations: immune rejection, poor cellular survival, and the limited spread of the injected cells (Lee et al., The Journal of Cellular Biology, Vol. 150, 2000, pp. 1085-1099). Lee further teaches:

> Skeletal muscle tissue has been extensively investigated as a potential source for isolation of pluripotent stem cells. A recent report has suggested that only a discrete minority of myoblast can survive after implantation and thus may represent a population of myogenic stem cells. In 1998, a specific population of highly purified muscle derived cells by the pre-plate technique that significantly improved cell survival after transplantation when injected intramuscularly. Although the mechanism by which these specific muscle derived cells display a high cell survival is unclear (page 1086).
> Comparison of the muscle-derived cells to other types of muscle-derived cells indicates that more studies are required to accurately assess the origin and more importantly, the functional property of these various populations of muscle-derived stem cells (page 1096-1097).

In addition, the art of record teaches that "the study of muscle satellite cells as a stem cell and it role in skeletal muscle is still in its infancy and it will now be important to characterize the

influence of growth factors and components of the extracellular matrix responsible for activating genetic responses within stem cells (Seale et al., Developmental Biology, 2000, page 122, IDS). Thus, at the time the application was filed, the state of the art for the production or isolation of a genus of muscle-derived progenitor cells having long-term survivability was considered unpredictable.

The specification provides working examples briefly described below:

Example 1 teaches the preparation of mouse muscle derived cells (MDC), pp6 (pages 28-30). Examples 3-5 and 7-8 display that genetically modified MDC with Lac Z were viable for up to 4 weeks in the lower abdomen of rats as shown in Example 3 (pages 32-33 and 39-40). Example 6 displays an increase in the contraction amplitude and contraction velocity of bladder strips of cryodamaged bladder tissue in rats using MDC (pages 33-39). Example 9 displays that genetically modified mc13 cells with adBMP-2 can cause bone formation (pages 40-51).

In view of the In re Wands Factors, the disclosure provides sufficient guidance for one skilled in the art to make murine and rat pp6 cells and the clonal muscle-derived cells, mc13 from murine pp6. However, in view of the lack sufficient guidance provided by the specification for making the genus of mammalian muscle-derived cells and the art of record stating that the functional properties of the various populations of muscle-derived cells require further research (Lee, pages 1096-1097); it is not apparent if cells from a different species with the same phenotypic markers would exhibit the same mechanisms because of the different markers displayed by other species.

Furthermore, with respect to cell markers, the art of record further teaches that:

> The expression of CD34 is reversible on hematopoietic stem cells. In fact, the art suggest that CD34 is probably a marker of activated stem cells, but it is not necessarily expressed

> in all stem cells. Although the reversible expression of CD34 remains to be determined in muscle derived stem cells, the use of CD34 as a marker of muscle-derived stem cells should at least by used with caution. Cells isolated at pp2 in our experiments are highly different than the cells isolated at pp6 in term of marker expression in vitro as well as their functional properties in vivo, see Qu and Lee.
>
> Progenitor cells give rise to related types of cells-lymphocytes, such as T cells, B cells, and natural killer cells, for example-but in their normal state do not generate a wide variety of cell type as such are not truly stem cells. It is necessary to show that the adult stem cell give rise to cell types that normally occur in different tissue. Neither of these criteria are easily met. (NIH: News: Stem Cells; Scientific Progress and Future Research Directions [online], June 2001, Executive Summary, ES-3, Appendix D, D-11 and D-12, and Chapter 4, page 23-25, 36, and 38, http:/www.nih.gov.news/stemcell/scireport.htm, retrieved online 5/15/02).

The pp6 cells displayed several markers (see Table 1), including Flk-1 a mouse homologue of human KDR gene, which was recently identified as a marker of hematopoietic cells with stem-like characteristics. In view of the specification and art of record it appears that the pp6 cells have different markers than other mammalian species, therefore, the pp6 cells would not be in other species. Thus, in view of the In re Wands Factors, it would require an undue amount of experimentation for one skilled the art to reasonably extrapolate from making and using pp6 cells from a mouse or a rat to making and using a genus of claimed muscle-derived progenitor cells.

With respect to the claimed methods (claims 17-26,45-54, 92-93, 102-104), the specification only enables one skilled to use murine or rodent pp6 cells for muscle therapy in mice or rats since the specification only provides sufficient guidance for making murine or rat pp6 cells. It would take one skilled in the art an undue amount of experimentation to reasonably correlate from the working examples to any claimed therapeutic method in any mammal other than mice or rats (e.g. method of treating weakness or dysfunction in muscle tissue in any mammal using muscle derived cell therapy) because of the lack of guidance for making other types of mammalian MDCs. Furthermore, the as-filed specification does not provide sufficient

guidance for one skilled in the art to reasonably extrapolate from using murine or rat pp6 cells for treating a muscle disorder in rodents or mice to treating any other mammal embraced by the claimed invention because of the problem (e.g., immune rejection, poor cellular survival, and the limited spread of the injected cells) with using mouse or rodent pp6 cells in other mammals (e.g. human). Furthermore, the as-filed specification fails to provide teaching what would be the appropriate dose of muscle-derived cells per route of administration for a sustained and high enough level of expression of transplanted cells in any other mammal. The art of record displays the unpredictability of muscle-derived cells differentiating into a specific muscle tissue. Kasemkijwattana et al. (IDS, Cell Transplantation, 1998) discloses that although muscle injury is capable of healing, an incomplete functional recovery often occurs (abstract) and the best treatment for muscle injury has not yet been define and the recommended treatment regimens for contusions have varied widely, depending on the severity of the injury (page 585). Furthermore, Ledley, *Pharmaceutical Research*, Vol. 13, pp. 1595-1614, 1996, discloses that "while transplantation of hepatocytes, pancreatic cells, myoblasts, epidermal cells, neuronal cells, synovial cells, and fibroblasts has been demonstrated in animals, these methods are not routinely available for treating any medical disease or disorder in any animal including humans (page 1596)." In the absence of essential teachings specific to the making and using a genus of mammalian muscle-derived progenitor cells, it would require an undue amount of experimentation for one skilled in the art to reasonably extrapolate from the disclosure to the treatment of any type of muscle disorder in any mammal other than mice or rats. Therefore, it would require an undue amount of experimentation for one skilled in the art to practice the full breadth of the claimed invention.

In conclusion, the as-filed specification and claims coupled with the state of the art at the time the invention was made only provide sufficient guidance and/or evidence to reasonably enable for isolated murine muscle-derived progenitor cells, wherein the cells are pp6 and express cell markers selected from the group consisting of desmin, CD34, Sca-1, Flk-1, and Bcl-2 and do not express CD45 and c-Kit and using the cells in a method of augmenting or bulking muscle in a rat or a mouse; and isolated clonal murine muscle-derived progenitor cells (mc13), wherein the clonally isolated cells express desmin, Flk-1, Sca-1 and does not express CD34, CD45, and c-Kit and not for the full scope of the claimed invention. One skilled in the art would have to engage in a large quantity of experimentation in order to practice the claimed invention based on the application's disclosure, the unpredictability of making and using mammalian muscle-derived progenitor cells with long-term survivability with any phenotype (cell marker) selected from the group consisting of desmin, CD34, Bcl-2 and Sca-1 or Flk-1, and the problems of using mouse or rat pp6 cells for treating muscle disorders in other types of mammals.

Applicant's arguments filed 11/21/02 have been fully considered but they are not persuasive. The as-filed specification only teaches how to make and use murine and rat pp6 cells in the claimed invention and breadth of the claims encompass making and using a genus of mammalian muscle-derived progenitor cells. One cell marker (Flk-1) found on pp6 murine cells is not found on other types of mammalian cells and the art of record displays concern with using the CD34 marker. The as-filed specification does not provide sufficient guidance or factual evidence for one skilled in the art to reasonably extrapolate from murine pp6 to a genus of mammalian muscle-derived progenitor cells with long-term survivability. Furthermore, the art of record teaches the unpredictability of isolating a genus of mammalian muscle-derived

progenitor cells with long-term survivability. Thus, in view of the In Re Wands Factors, the as-filed specification does not provide sufficient guidance or factual evidence for one skilled in the art to make and use a genus of mammalian muscle-derived progenitor cells with long-term survivability.

The as-filed specification does not provide sufficient guidance and/or factual evidence for how to overcome unpredictability of making and using a genus of mammalian muscle-derived progenitor cells.

In addition, the court in Enzo 188 F.3d at 1374, 52 USPQ2d at 1138 states:

> It is well settled that patent applications are not required to disclose every species encompassed by their claims, even in an unpredictable art. However, there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed.
> In re Vaeck, 947 F.2d 48, 496 & n.23. 30 USPQ2d 1438, 1445 &n23 (Fed. Cir. 1991)(citation omitted). Here, however, the teachings set forth in the specification provide no more than a "plan" or "invitation" for those of skill in the art to experiment...; they do not provide sufficient guidance or specificity as to how to execute that plan. See Fiers v. Revel. 984 F.2d.1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993); In re Wright, 999 F.2d...[1557], 1562, 27 USPQ2d...[1510], 1514. [footnote omitted].

On this record, it is apparent that the specification and the applicants' traversal (See page 7 of traversal, which states, "applicants have described a means to assess whether isolated MDC are viable and proliferate and survive as claimed by injecting into cells into SCID mice") provide no more than a plan or invitation in view of the art of record exemplifying the unpredictability of using any progenitor cell in the claimed methods of cell therapy for treating a muscle disorder in a mammal, for those skilled in the art to experiment with progenitor cells so as to provide isolated mammalian muscle-derived progenitor cells as intended by the as-filed specification at the time the invention was made.

See also Genetech Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1366, 42, USPQ2d 1001, 1005 (Fed. Cir. 1997)

> ("Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable the public to understand and carry out the invention.")

In view of the art of record and the lack of guidance provided by the specification; the specification does not provide reasonable detail for what protocols are required for different types mammalian muscle-derived progenitor cells other than pp6 from rat and mice, and it would take one skilled in the art an undue amount of experimentation to reasonably extrapolate from the scope listed above to the full scope of claimed invention.

The Declaration of Michael Chancellor, M.D. under 37 CFR 1.132 filed 11/21/02 is insufficient to overcome the rejection of claims 1, 3, 17-26, 45-54, 84, 92-93, 96, and 100-106 based upon 112 first paragraph enablement as set forth in the last Office action because: In view of the In Re Wands Factors and the reasons set forth above, the as-filed specification does not provide sufficient guidance for one skilled in the art to make and use a genus of mammalian muscle derived progenitor cells. Also see Genetech Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1366, 42, USPQ2d 1001, 1005 (Fed. Cir. 1997) and in Enzo 188 F.3d at 1374, 52 USPQ2d at 1138.

The rejection of claims 1, 84, and 94 under 35 U.S.C. 112, second paragraph is moot in view of the cancellation of claim 94 and the amendment to claims 1 and 84.

Double Patenting

The non-statutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper time-wise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3, and 84 remain and claims 100, 101, and 106 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 76-80 of co-pending Application No. 09/302,896. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of co-pending application '896 are drawn to a method of isolating and purifying muscle-derived stem cells, comprising: a) plating dissociated muscle cells on a collagen-coated substrate; b) isolating muscle derived cells populations which adhere to said substrate at successive time intervals following said plating step a); and c) determining the characteristics of the isolated cell population to identify muscle-derived stem cells (claim 76). In addition, the claims are drawn to the method described above, wherein said cells express one or more markers selected from BCL-2, CD34, and desmin (claim 79).

Although the conflicting claims in the instant application and co-pending application '896 are not identical, they are not patentably distinct from each other because each invention encompasses the same material and the patents use the muscle derived cells encompassed in the

instant application. The difference between the claims of the instant application and co-pending application '896 is that the instant application encompasses more descriptive steps of the isolation process of muscle-derived cells. Therefore, the claims of the instant application and co-pending application '896 are obvious variants of one another.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's arguments filed 11/21/02 have been fully considered but they are not persuasive because the applicants have not provided sufficient evidence to overcome the provisional double patenting rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claim 106 is rejected under 35 U.S.C. 102(e) as being anticipated by Anderson et al. (US Patent No. 6,001,654, EFD 4/25/97). Anderson teaches isolated smooth muscle progenitor cells (column 13, lines 23-26 and column 16, lines 53-67).

Applicants' traversal is not applicable to the new rejection under 102(e).

Claim 106 is rejected under 35 U.S.C. 102(b) as being anticipated by Huard et al. (IDS, Muscle & Nerve, pages 224-234, 1994). Huard teaches human myoblasts obtained from a postmortem biopsy of a 13 month-old boy (page 225).

Applicants' traversal is not applicable to the new rejection under 102(b).

The provisional 103(a) rejection for claims 1, 3, 84, 94-95 is moot in view of applicant's traversal. See pages 21-22.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader, SPE - Art Unit 1635, can be reached at (703) 308-0447.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER

Brian Whiteman
Patent Examiner, Group 1635